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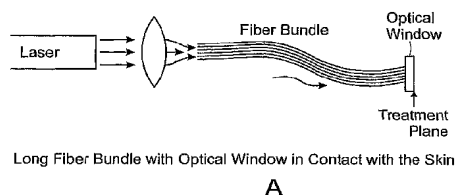
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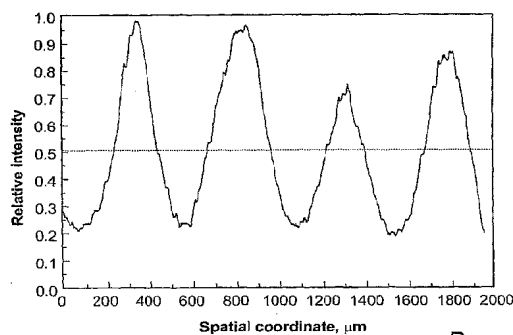
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(54) Title: METHODS AND SYSTEMS FOR LASER TREATMENT USING NON-UNIFORM OUTPUT BEAM



A



B

(57) Abstract: Methods and apparatus for treatment, such as skin rejuvenation treatment, use non-uniform laser radiation. A high-intensity portion of the laser radiation causes collagen destruction and shrinkage within select portions of the treatment area, while a lower-intensity portion of the radiation causes fibroblast stimulation leading to collagen production across other portions of the treatment area. An output beam from a laser source, such as an Nd:YAG laser, is coupled into an optical system that modifies the beam to provide a large-diameter beam having a nonuniform energy profile, comprised of a plurality of high-intensity zones surrounded by lower-intensity zones within the treatment beam. The higher-intensity zones heat select portions of the target tissue to temperatures sufficient for a first treatment (e.g. collagen shrinkage), while the lower-intensity zones provide sufficient energy for a second treatment (e.g. stimulated collagen production). A large area of tissue, preferably 7-10 mm in diameter, can be treated simultaneously, while minimizing the risk of burning or other damage to the skin. In one embodiment, the invention uses a fiber bundle to provide a non-uniform energy output beam, hi another embodiment, the invention uses a diffractive lens array to produce the non-uniform output beam. A cooling system can also be integrated with the laser treatment system. A pulse light source can also be integrated with the laser treatment system in a combined skin rejuvenation therapy.



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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

-1-

## METHODS AND SYSTEMS FOR LASER TREATMENT USING NON-UNIFORM OUTPUT BEAM

### RELATED APPLICATION

This application is a continuation-in-part of U.S. Application  
5 No. 11/347,672, filed February 3, 2006, which claims the benefit of U.S. Provisional  
Application No.: 60/673,914, filed April 22, 2005, the entire teachings of which are  
incorporated herein by reference.

### BACKGROUND OF THE INVENTION

Plastic surgeons, dermatologists and their patients continually search for new  
10 and improved methods for treating the effects of an aging skin. One common  
procedure for rejuvenating the appearance of aged or photodamaged skin is laser  
skin resurfacing using a carbon dioxide laser. The carbon dioxide laser energy is  
absorbed by tissue water causing vaporization of the outer skin layer. Carbon  
dioxide lasers have been utilized for approximately three decades. However it has  
15 only been the past few years that these lasers have been arranged to remove only thin  
tissue layers with minimal heat damage to the surrounding skin. While carbon  
dioxide lasers may remove about 150 microns of skin, that skin may take a month or  
more to heal under such a procedure.

Er:YAG lasers have been utilized to ablate even thinner layers of tissue than  
20 carbon dioxide layers. However they lack the coagulation characteristics and thus  
allow more bleeding than a carbon dioxide laser during use.

Non-ablative skin rejuvenation is a methodology which does not take the top  
layer of skin off, but which uses a deep-penetrating laser to treat the layers of skin  
beneath the outer epidermal layer, treating unsightly vascular and pigmented lesions,  
25 and shrinking and modifying the underlying collagen, tightening the skin and  
reducing wrinkles to provide a more youthful appearance. This methodology  
however, has a low efficiency, and an aggressive cooling method must be used on to

-2-

the skin so as to minimize damaging the top or upper layer thereof and also to minimize pain generation. The “fluence” or energy density used is greater than 10 joules per square centimeter and to be more effective this fluence often reaches 30 Joules per square centimeter. This level of energy often causes pain and epidermal damage.

United States Published Patent Application No. 2002/0161357 A1, by Anderson *et al.*, discusses a method and apparatus for performing therapeutic treatment on a patient’s skin by using focused radiation beams to create “islands” of treatment/damage within untreated portions of the patient’s skin. However, the parameters of the treatment beam in this method are not optimal for skin rejuvenation treatment.

Yet another treatment method is disclosed in U.S. Patent No. 6,077,294 to Cho *et al.*, the entire teachings of which are incorporated herein by reference. This patent describes a system and methodology for noninvasive skin treatment that utilizes a pulsed dye laser having a wavelength of about 585 nanometers (nm), and an energy of less than 5 Joules per square cm. In contrast to earlier techniques which used higher-energy pulses to damage and “shrink” the collagen below the epidermis, the relatively lower energies of the beams in the ‘294 patent are designed to stimulate the collagen to regenerate and “fill in” valleys of the skin for a younger more clearer skin.

## SUMMARY OF THE INVENTION

The present invention relates to methods and apparatus for treatment using non-uniform laser radiation. Preferably, the invention is used for skin rejuvenation treatment, in which a high-intensity portion of the laser radiation causes collagen destruction and shrinkage within select portions of the treatment area, while a lower-intensity portion of the radiation causes fibroblast stimulation leading to collagen production across other portions of the treatment area.

Preferably, the method and system of the invention utilize a solid-state laser source, such as an Nd:YAG laser. The output beam from the laser source is coupled into an optical system that modifies the beam to provide a large-diameter beam

having a non-uniform energy profile, comprised of a plurality of high-intensity zones surrounded by lower-intensity zones within the treatment beam. The higher-intensity zones heat select portions of the target tissue to temperatures sufficient for a first treatment (*e.g.* collagen shrinkage), while the lower-intensity zones provide  
5 sufficient energy to the surrounding tissue for a second treatment (*e.g.* stimulated collagen production). Thus, a large area of tissue, preferably 7-10 mm in diameter, can be treated simultaneously, while minimizing the risk of burning or other damage to the skin.

In one embodiment, the invention uses a fiber bundle to provide a non-uniform energy output beam. In another embodiment, the invention uses a  
10 diffractive lens array to produce the non-uniform output beam.

A method of treating human skin in accordance with one aspect of the invention comprises generating an output beam from a laser source, such as an Nd:YAG laser; coupling the beam into an optical system that modifies the beam to  
15 provide a treatment beam having a non-uniform energy profile, the treatment beam comprised of a plurality of high-intensity zones surrounded by low-intensity zones within the treatment beam; and directing the treatment beam to a target tissue area such that the high-intensity zones heat select portions of the target tissue to temperatures sufficient for a first treatment, while the lower-intensity zones provide  
20 sufficient energy to the surrounding tissue for a second treatment. Preferably, the first treatment comprises collagen shrinkage and the second treatment comprises collagen stimulation. The output beam can have a wavelength between about 1.3 to 1.6 microns, and preferably between about 1.41 and 1.44 microns, and a pulse duration between 0.1 and 100 milliseconds, and preferably between about 1 and 5  
25 milliseconds. The average fluence of the treatment beam can be less than about 10 J/cm<sup>2</sup>. Generally, the average fluence of the treatment beam is between about 5-6 J/cm<sup>2</sup>. The average fluence in the lower-intensity zones is generally on the order of 2-3 J/cm<sup>2</sup>.

The optical system can comprise a fiber bundle, having 1000 to 2000  
30 separate fibers, for instance, and a focusing lens for coupling the beam into the fiber bundle. An optical window, preferably between 1 and 5 mm thick, can be located at

-4-

the distal end of the bundle, the optical window permitting the beams emitted from each fiber in the bundle to diverge and partially overlap with one another before they reach the target tissue. In certain embodiments, a transport fiber can carry the output beam from the laser source to the fiber bundle, and the fiber bundle can be located in  
5 a handpiece.

In another embodiment, the optical system can comprise a diffractive lens array, preferably comprised of about 2000 or less lenses, arranged in an optical path between a laser source and the treatment area, such that each lens in the array provides a high-intensity zone surrounded by a low intensity zone of radiation. Each  
10 lens in the array can have a diameter of between about 150 and 450 microns, and the entire lens array can have a diameter of between about 7 and 10 mm. Preferably, the average fluence of the laser output beam is less than about 10 J/cm<sup>2</sup>.

In another embodiment, a laser system of the invention comprises a laser source that generates an output beam; and an optical system that modifies the output  
15 beam to provide a treatment beam having a non-uniform energy profile, the treatment beam being comprised of a plurality of high-intensity zones surrounded by low-intensity zones within the treatment beam, such that the high-intensity zones heat select portions of a target tissue to temperatures sufficient for a first treatment, while the lower-intensity zones provide sufficient energy to the surrounding tissue  
20 for a second treatment. The laser source can be an Nd:YAG laser, and generally produces an output beam having a wavelength between about 1.3 to 1.6 microns, and preferably between about 1.41 and 1.44 microns, and a pulse duration between 0.1 and 100 milliseconds, preferably between about 1 and 5 milliseconds. The optical system can comprise a fiber bundle, preferably with an optical window between the  
25 distal end of the bundle and the target tissue. Alternatively, the optical system can include a diffractive lens array in the optical path between the source and the treatment area, such that each lens in the array provides a high-intensity zone surrounded by a low intensity zone of radiation.

According to another embodiment, a laser system comprises a laser source  
30 that generates an output beam; a fiber bundle comprising a plurality of individual fibers, the fiber bundle having a proximal end and a distal end; a focusing lens for

-5-

coupling the output beam into a proximal end of the fiber bundle; and an optical window at the distal end of the fiber bundle, the optical window permitting the beams emitted from each fiber in the bundle to diverge as the beam passes through the optical window so that each beam partially overlaps with the beam(s) from adjacent fibers in the bundle. The optical window can comprise a transparent material, such as glass, or could comprise a spacer having an empty space between the distal end of the fiber bundle and the treatment area.

According to yet another embodiment, a laser system comprises a laser source that generates an output beam; and a diffractive lens array arranged in an optical path between a laser source and a treatment area, such that each lens in the array provides a high-intensity zone surrounded by a low intensity zone of radiation.

In certain embodiments, a laser system and method of the invention comprises a tip housing that contains the optical system for providing a treatment beam having a non-uniform energy profile, a distal end of the tip housing being adapted to contact against the target tissue area of the patient; and a conduit that carries cooled air to the tip housing, the conduit comprising an outlet that is angled to direct cooled air onto the distal end of the tip housing.

In further embodiments, a laser system of the invention further comprises a pulse light system, such as a flashlamp system, integrated with the laser system, for treating pigmented lesions.

The present invention provides a laser treatment which covers a large area of the patient, is characterized by high-absorption of the laser radiation and lower peak energies, which results in minimal risk of skin damage. In one aspect, the present invention advantageously accomplishes stimulated collagen production as well as collagen shrinkage simultaneously in a single treatment area. In addition to skin rejuvenation treatment, the principles of the invention can also be extended for use in other types of optical radiation treatments, including, without limitation, treatment of acne, hair removal, and treatment of vascular or pigmented lesions.

## BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention, as illustrated in the accompanying drawings in which  
5 like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention.

Fig. 1A illustrates a laser treatment system comprising a fiber bundle and optical window;

10 Fig. 1B is a plot of the beam profile on the skin for the laser treatment system of Fig. 1A;

Fig. 2 illustrates a laser treatment system comprising a short fiber bundle with expanded distal face;

Fig. 3 shows a diffractive lens having four levels;

15 Fig. 4 shows a diffractive lens having two levels;

Fig. 5 shows a diffractive lens with eight levels;

Fig. 6 shows a diffractive lens array having a hexagonal pattern;

Fig. 7 shows a diffractive lens array having an elongated hexagonal pattern;

Fig. 8 shows a treatment beam profile for a diffractive lens array;

20 Fig. 9 shows a plot of the relative hot area fluence factor,  $F_1/F_{av}$ , as a function of the relative diameter of the central hot area,  $d/D$  for a diffractive lens array in accordance with one aspect of the invention;

Fig. 10 shows the temperature profile of skin treated with a non-uniform output beam from a diffractive lens array;

25 Fig. 11 shows a tip of a laser treatment handpiece having a cooling mechanism; and

Fig. 12 shows an integrated laser and pulse light system for skin rejuvenation treatment.

## DETAILED DESCRIPTION OF THE INVENTION

30 A description of preferred embodiments of the invention follows.



-7-

As shown in Fig. 1A, the apparatus includes a laser source that emits an output beam. The beam is coupled into a bundle of optical fibers using one or more focusing lenses. The bundle preferably contains between 1000 and 2000 separate fibers. Typically, each fiber has a diameter of about 100-200 microns. The output  
5 laser beam is thus directed to 1000-2000 smaller beams, each of which traverses the length of the fiber bundle in individual optical fibers. The fiber bundle terminates at its distal end at an optical window that can be held in direct contact with the patient's skin. The window is approximately 1-5 mm thick, and protects the output face of the fiber bundle from contamination, and also permits the beam emitted from  
10 each fiber to diverge before it reaches the patient's skin, preferably so that each beam partially overlaps with the beam(s) from adjacent fibers in the bundle.

The fibers in the bundle can be packed together tightly, or can be spaced apart from each other using mechanical spacers. The use of mechanical spacers at the distal end of the bundle spreads the energy from the bundle over a larger area,  
15 and helps to reduce the pain sensation for the patient. In general, the combined spot size on the skin from all the fibers in the fiber bundle is between approximately 7 and 10 mm in diameter.

In a preferred treatment method for the embodiment of Fig. 1A, the laser source, which is preferably an Nd:YAG laser, produces an output laser pulse having  
20 a wavelength of between 1.3 and 1.6, preferably between about 1.40 and 1.44 microns, and a pulse duration of between 0.1 and 100 milliseconds, preferably between about 1 and 5 milliseconds. Because the laser operates at wavelengths that are well-absorbed by the skin, the laser can operate at relatively low energies, and minimize the risk of burning or damage to the skin.

25 In operation, the optical window is held against the skin of the patient, and the laser source is energized to produce a pulse of laser light that travels from the source through the fiber bundle and the optical window, and penetrates into the patient's skin. Since the optical window is approximately 1-5 mm thick, the window also serves as a spacer between the output end of the fiber bundle and the skin of the  
30 patient. Thus, as the laser light is emitted from each fiber in the bundle, the light is permitted to diverge as it travels through the window to the patient's skin. In a

preferred embodiment, the fibers are approximately 100-200 microns in diameter, and the beam emitted from each fiber, after passing through the window, produces a spot between 150-900 microns in diameter on the patient's skin. Because of the diverging nature of light emitted from an optical fiber, the light at the center of each spot will be relatively high-energy light, while the light at the periphery of each spot will have significantly lower energy. Thus, over a combined spot size of 7 to 10 mm for the entire fiber bundle, there are approximately 1000 to 2000 smaller treatment spots, generally about 150-900 microns in diameter, each consisting of a higher-fluence "hot spot" at the center of the spot surrounded by a lower-fluence "cooler zone" of radiation. The energy at the central "hot spot" is sufficient to shrink the underlying tissue, damage the collagen and produce collagen shrinkage. In general, the energy at the high-intensity zones, or "hot spots" is sufficient to raise the temperature of the target tissue to 70° C or higher. However, the radiation in "cooler zone" surrounding the hot spot is generally not sufficient to damage the tissue and cause collagen shrinkage in the tissue underlying these areas. In these lower-intensity "cooler zones," the energy provided will only raise the temperature of the skin by a few degrees (or perhaps result in no appreciable temperature rise), and thus will not damage or even "shock" the tissue. However, this lower-intensity radiation is generally more appropriate or preferred to stimulate the fibroblasts in the tissue to produce collagen and "fill in" the skin for a younger more clearer skin

In a preferred embodiment, the fibers in the bundle are arranged so that the spot sizes of radiation from each fiber about or partially overlap with the spots from the adjacent fibers in the bundle on the patient's skin. In this way, the invention can simultaneously provide two modes of skin rejuvenation treatment: higher-energy collagen shrinkage treatment in the "hot spots" at the center of each output spot from the fiber bundle, and overall stimulated collagen production throughout the entire area of the combined fiber-bundle output beam.

An example of a laser treatment method using a fiber bundle delivery system is illustrated in Fig. 1B, which is a plot of the relative intensity on the skin as a function of location on the skin for four fibers in the bundle. In practice, the fiber bundle will consist of 1000-2000 individual fibers, in a regularly-spaced

arrangement to form a bundle. In this embodiment, the center-to-center distance between adjacent fibers in the bundle is approximately 500 microns. The diameter of each fiber is approximately 200 microns, and the numerical aperture (NA) of the fibers is approximately 0.2. The total diameter of the fiber bundle is approximately 9 millimeters. The laser energy emitted from each fiber diverges as it passes through the transparent window, so that the spot size on the skin from each fiber is at least about 250 microns in diameter. Thus, the spots from each fiber generally abut or partially overlap with the spots from the adjacent fibers in the bundle. This is shown in Fig. 1B, where it can be seen that the whole area is treated with at least a low-intensity pulse, while the areas at the center of each spot receive a significantly higher dose of energy. The dotted line represents the average intensity throughout the treatment area. In this example, the peak fluence on the skin at the center of each spot is approximately  $9 \text{ J/cm}^2$ , while the fluence at the periphery of each spot is approximately  $2 \text{ J/cm}^2$ . The total area fluence is approximately  $5 \text{ J/cm}^2$ .

The fluence(s) received at various portions of the treatment area can be varied and controlled by, for instance, raising or lowering the total energy output from the laser source, changing the center-to-center distances between fibers in the bundle, using different diameter fibers, using fibers with a different NA to change the divergence of the beam and/or altering the thickness of the optical window to allow for a greater or lesser amount of beam divergence. The beam profile can thus be optimized for a variety of different conditions and laser treatment methods.

Fig. 2 shows yet another embodiment that is similar to the embodiment of Fig. 1, except that instead of a long-fiber bundle coupling the laser output beam from the source to the optical window, this embodiment uses a single transport fiber to carry the laser energy from the laser source to a handpiece containing a shorter fiber bundle. At the handpiece, the output laser pulse from the single fiber is coupled into the short fiber bundle. As in the prior embodiment, the short fiber bundle is comprised of a plurality of separate optical fibers, preferably 1000 to 2000 fibers. The short fiber bundle has a smaller bundle diameter at its proximal end to allow the output light from the single transport fiber to efficiently couple into the bundle. The fiber bundle "fans out" from its proximal end to its distal end, using, for example,

-10-

mechanical spacers, to provide an expanded face at its output. Preferably, the expanded face has a diameter of between approximately 7 to 10 mm, and is coupled to an optical window, as in the embodiment of Fig. 1. The embodiment of Fig. 2 preferably uses the same treatment parameters as those described in connection with Fig. 1.

Turning now to Figs. 3-8, yet another embodiment of the invention is illustrated which uses a diffractive lens array to provide non-uniform heating in the target tissue. A multilevel diffractive lens consists of a number of concentric rings made of optically transparent material with variable thicknesses. The top surface of each concentric ring is flat so the refractive effects are negligible. The variable-thickness rings give rise to a spatial phase delay pattern on a propagating incident optical beam. The propagating optical beam carries the spatial phase delay pattern past the plane of the diffractive lens and produces an illumination pattern of spatially variable optical intensity. The optical intensity is high at geometrical points that meet the conditions for constructive interference and low at the points that meet the conditions for destructive interference. In general the design of a diffractive lens is optimized so that the principal diffraction maximum (or minimum) would be on the optical axis at a distance  $f$  from the plane of the lens. The distance  $f$  is the focal length of the lens. In general the goal of the diffractive lens design is to increase the fraction of the incident power in the principal diffraction maximum. However, that fraction is always less than 1 depending on the number of levels, the  $F$ -number of the lens and other design parameters. In fact, it is possible to design the diffractive lens pattern so that any fraction (less than 1) of the incident power would be in the principal maximum and the rest of the power would be distributed in the secondary maxima.

Various examples of multi-level diffractive lenses are shown in cross-sectional views in Figs. 3-5. Fig. 3 shows a diffractive lens having four levels; Fig. 4 shows a diffractive lens having two levels; and Fig. 5 shows a diffractive lens with eight levels.

In one embodiment of the present invention, a laser treatment apparatus and method utilizes plurality of diffractive lenses that are arranged in an array to produce

an output beam having a non-uniform energy profile. More specifically, the diffractive lens array is arranged in an optical path between a laser source and the treatment area, such that each lens in the array provides for an area of higher-fluence “hot spots” surrounded by lower-fluence regions of radiation. In a skin rejuvenation treatment, for example, the higher-energy areas provide sufficient heating to damage and shrink collagen in the “hot spots,” while the lower-intensity radiation regions outside of these hot spots overlap and combine to stimulate collagen regrowth over the entire treatment area.

In this embodiment, the laser source preferably produces a pulse of radiation having a wavelength between approximately 1.3 and 1.6 microns, preferably between 1.40 and 1.44 microns, and a pulse duration of between about 0.1 and 100 milliseconds, preferably between 1 and 5 milliseconds. The laser source can be an Nd:YAG laser, for example. An optical system carries the beam from the laser source to the treatment area. The diffractive lens array is preferably arranged at the distal end of the optical system, adjacent to the patient’s skin. The array comprises a plurality of separate diffractive lenses adjacent to one another. In general, there are 2000 or less lenses in an array, and preferably about 1800 lenses. Each lens is between about 150 and 450 microns in diameter, and is preferably about 250 microns in diameter. The entire array of diffractive lenses is generally about 7 to 10 mm in diameter. The array directs the input beam from the laser source (which is preferably also about 7-10 mm in diameter) into a plurality of higher-intensity “hot spots,” corresponding to the central portion of each individual lens in the array, and lower intensity regions surrounding each hot spot. The combined effect in the patient’s tissue is to produce a plurality of higher-intensity zones in the skin corresponding to the center of each diffractive lens surrounded by areas of lower-intensity radiation. This is shown in the treatment beam profile of Fig. 8. As can be seen in this graph, the entire treatment area receives at least a low level of treatment radiation, with certain spaced-apart portions receiving a higher dose of laser radiation. In the case of skin rejuvenation, for example, the laser energy penetrates deep into the collagen layer, where the collagen is heated to shrinkage temperatures in the “hot spots,” while the entire treatment area is treated to effect collagen

-12-

regeneration. In addition to skin rejuvenation treatment, the diffractive lens array can be optimized for use in other applications, such as treatment of acne and hair removal. A different beam profile from the diffractive lens array can be used for different applications.

- 5           The diffractive lens is considered to be irradiated by an average uniform fluence,  $F_{av}$ , determined by the laser fluence setting selected by the user. In general, the average fluence of the laser in this embodiment is less than about 10 J/cm<sup>2</sup>, and is preferably about 9 J/cm<sup>2</sup>. For purposes of illustration, each diffractive lens with diameter  $D$  is assumed to have a simplified design so that it produces a hot area with
- 10   diameter,  $d$ , assumed to have uniform fluence,  $F_1$ , and a periphery having a uniform fluence,  $F_2$ . The lens design is assumed to produce a fluence ratio,  $\beta$ , of the hot area versus the periphery,  $\beta = F_1/F_2$ . Under these simplifying assumptions, is it possible to derive a simple formula to approximate the hot area fluence,  $F_1$ :

$$\frac{F_1}{F_{av}} = \frac{1}{\left(\frac{d}{D}\right)^2 + \frac{1}{\beta} \left[1 - \left(\frac{d}{D}\right)^2\right]} \quad (\text{Eq. 1})$$

- 15   Fig. 9 shows a plot of the relative hot area fluence factor,  $F_1/F_{av}$ , as a function of the relative diameter of the central hot area,  $d/D$ . As an example, if the diffractive lens is designed to have  $\beta = 5$ , with diameter  $D = 250 \mu\text{m}$ , hot area diameter  $d = 100 \mu\text{m}$ , and the laser is selected to have average fluence  $F_{av} = 9 \text{ J/cm}^2$ , then the hot area fluence is  $F_1 = 3.05 \times 9 \text{ J/cm}^2 = 27.4 \text{ J/cm}^2$ .

- 20           As a second example, if the diffractive lens is designed to have  $\beta = 5$ , with diameter  $D = 350 \mu\text{m}$ , hot area diameter  $d = 200 \mu\text{m}$ , and the laser is selected to have average fluence  $F_{av} = 9 \text{ J/cm}^2$ , then the hot area fluence is  $F_1 = 2.17 \times 9 \text{ J/cm}^2 = 19.5 \text{ J/cm}^2$ .

- Figs. 6 and 7 illustrate two exemplary embodiments of a diffractive lens
- 25   array according to the invention. In Fig. 6, the diffractive lenses are arranged in a

hexagonal pattern. In Fig. 7, the lenses are arranged in an elongated hexagonal pattern.

Fig. 10 shows the peak tissue temperature distribution for a portion of skin irradiated with a 1440 nm laser through a diffractive lens array. As can be seen from the graph, a first diffractive lens is centered at about 200  $\mu\text{m}$ , and a second diffractive lens is centered at about 600  $\mu\text{m}$  on the horizontal axis. As can be seen from this graph, there is an area of tissue about 200  $\mu\text{m}$  wide centered on each of the diffractive lenses that is heated to relatively high peak temperatures (*e.g.*, 70° C or higher). This high-temperature zone extends from essentially the surface of the skin to a depth of about 350  $\mu\text{m}$ . As discussed above in connection with the fiber-bundle embodiment of Figs. 1A and 1B, these temperatures are sufficient to cause collagen shrinkage. Outside of these high-temperature treatment zones, the peak temperatures quickly drop off. For example, in the area between about 300  $\mu\text{m}$  and 500  $\mu\text{m}$  on the horizontal axis, the peak skin temperatures are generally between 35° C (or less) and 50° C, and are generally less than about 40° C. As previously discussed, these lower intensity zones provide collagen stimulation treatment.

Fig. 11 is a cross-sectional view of a tip 10 of a laser treatment apparatus having a diffractive lens array for providing an output beam having a non-uniform energy profile. The operator applies the tip 10 directly against the patient's skin 30. A laser source (not shown) is energized to produce an output beam 23, and the output beam is carried to the tip 10 by an optical fiber 20. The output beam 23 is emitted from the end of optical fiber 20, and is directed to diffractive lens array 61. Adjacent to the diffractive lens array 61 is an optical window 60 that directly contacts the patient's skin 30. The optical window 60 is similar to the optical window described in connection with Fig. 1, and functions as a spacer between the output end of the fiber bundle and the skin of the patient. The optical window 60 can be integral with the diffractive lens array 61. Preferably, the window is made of a good thermal conductive material, such as glass. The optical fiber 20, lens array 61, and optical window 60 are all enclosed in a tip housing 40, which is preferably a cylindrically-shaped housing. The tip housing 40 can be made of plastic. Outside the tip housing 40 is a cooling mechanism 11. Preferably, the cooling mechanism 11

comprises a conduit 50 that carries cooled air 51 from a cooled air source (not shown) to the tip 10 of the treatment apparatus. The conduit 50 preferably includes an outlet that is angled with respect to the tip housing 40, so that cooled air 51 is directed at the distal end of the tip housing 40 (*i.e.* where the tip 10 interfaces with the patient's skin 30). This arrangement provides effective cooling of the skin during laser treatment. Although the tip 10 and cooling mechanism 11 are shown here in connection with the diffractive lens array embodiment of Figs. 3-8, it will be understood that this design may also be employed with a laser apparatus having a fiber bundle, such as shown and described in connection with Figs. 1 and 2.

Fig. 12 shows an integrated laser and pulse light system for skin rejuvenation treatment, according to one aspect of the invention. As shown, the system 100 includes a housing 101 containing a laser source 103, preferably a solid-state laser, such as an Nd:YAG laser operating at about 1.4 microns wavelength and about 3 msec pulse width. Light from the laser source 103 is coupled into an optical fiber delivery system 20, which extends from the housing 101 to a first handpiece 105. The first handpiece 105 includes an optical system for producing a beam with a non-uniform energy profile, in accordance with any of the embodiments previously described herein. The handpiece 105 can include a tip 10 as previously described in connection with Fig. 11. The system can also employ a cooling system as described in connection with Fig. 11.

The integrated system 100 also includes a pulse light portion, that preferably includes a flashlamp light source 115. In a preferred embodiment, the flashlamp source comprises a Xenon flashlamp that produces treatment pulses having wavelengths between 560 and 950 nm and pulse widths between 5 and 35 milliseconds. The flashlamp 115 is located in a second handpiece 113 connected to the housing 101 by a high-voltage cable 111 that provides power to the flashlamp 115 from a high-voltage source 109 located within the housing 101. The pulse portion preferably also includes a water circulating system (not shown), as is conventionally known, for cooling the flashlamp. The pulse light system can also employ a cooling system as described in connection with Fig. 11. In one embodiment, an air cooler and conduit carry cold air to handpiece 115. The tip of



-15-

handpiece 115 includes a sapphire window. The edge of the proximal side of the sapphire window (*i.e.* the side closest to the flashlamp source) is cooled by the cold air from the cooling system. The distal surface of the sapphire window contacts the patient's skin for treatment.

5           In operation, the second handpiece 113 is held proximate to the patient's skin, and the flashlamp 115 is energized to provide a treatment pulse. The spot size of the pulse light portion is generally larger than the laser portion, and is generally around 11 x 55 mm (or 6 cm<sup>2</sup>). The pulse light portion is thus able to treat large areas of the patient's skin in a relatively short time period. The maximum fluence of  
10 the pulse light portion is typically around 20 J/cm<sup>2</sup>.

          The pulse light portion of the integrated system is well-suited to treat pigmented and certain vascular lesions. The pulse light portion effectively treats, for example, dischromia, a common condition associated with aging skin, as well as superficial pigmented lesions, veins, and the blush of rosacea associated with sun-  
15 damaged skin. The laser portion of the system is effective for stimulation of collagen production and skin tightening, as previously discussed. The combination of laser treatment and pulse light treatment in an integrated system provides a complete and efficient system for facial rejuvenation treatment. The laser and pulse light system(s) are integrated in a common housing, and preferably use a common  
20 control system 117, and can even use the same electronic drive circuit 119 for driving both the laser source 103 and the flashlamp source 115.

          While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without  
25 departing from the scope of the invention encompassed by the appended claims.

-16-

## CLAIMS

What is claimed is:

1. A method of treating human tissue, comprising:  
generating an output beam from a laser source;  
5 coupling the beam into an optical system that modifies the beam to provide a treatment beam having a non-uniform energy profile, the treatment beam comprised of a plurality of high-intensity zones surrounded by low-intensity zones within the treatment beam; and  
directing the treatment beam to a target tissue area such that the high-  
10 intensity zones heat select portions of the target tissue to a first temperature sufficient to shrink collagen, while the lower-intensity zones provide sufficient energy to the surrounding tissue to stimulate collagen production.
2. The method of Claim 1, wherein the treatment beam at the high-intensity zones heats select portions of the target tissue to a temperature of 70° C or  
15 higher.
3. The method of Claim 1, wherein the laser source comprises an Nd:YAG laser.
4. The method of Claim 1, wherein the wavelength of the output beam is between about 1.3 microns and 1.6 microns.
- 20 5. The method of Claim 4, wherein the wavelength of the output beam is between about 1.40 and 1.44 microns.
6. The method of Claim 1, wherein the treatment beam at the target tissue area has a diameter between about 7 and 10 mm.

-17-

7. The method of Claim 6, wherein the average fluence of the treatment beam at the target tissue area is less than about  $10 \text{ J/cm}^2$ .
8. The method of Claim 1, wherein the output beam has a pulse duration of between 0.1 and 100 milliseconds
- 5 9 The method of Claim 8, wherein the output beam has a pulse duration of between 1 and 5 milliseconds.
10. The method of Claim 1, wherein the optical system comprises a fiber bundle.
11. The method of Claim 10, wherein the fiber bundle comprises 1000 to 2000 fibers.
- 10 12. The method of Claim 10, wherein the optical system comprises a focusing lens for coupling the output beam into a proximal end of the fiber bundle, and an optical window between the distal end of the fiber bundle and the target tissue, the optical window permitting the beam emitted from each fiber in the bundle to diverge before it reaches the target skin so that each beam  
15 partially overlaps with the beam(s) from adjacent fibers in the bundle.
13. The method of Claim 12, wherein the optical window is between 1 and 5 mm thick.
14. The method of Claim 10, wherein the average fluence of the treatment beam is less than about  $10 \text{ J/cm}^2$ .
- 20 15. The method of Claim 10, wherein the optical system comprises a transport fiber that carries the output pulse from the laser source to a handpiece containing the fiber bundle.

-18-

16. The method of Claim 1, wherein the optical system comprises a diffractive lens array arranged in an optical path between a laser source and the treatment area, such that each lens in the array provides a high-intensity zone surrounded by a low intensity zone of radiation.
- 5 17. The method of Claim 16, wherein the diffractive lens array comprises about 2000 or less lenses in the array.
18. The method of Claim 17, wherein each lens is between about 150 and 450 microns in diameter.
19. The method of Claim 16, wherein the diffractive lens array is between 7 and  
10 10 millimeters in diameter.
20. The method of Claim 16, wherein the average fluence of the laser output beam is less than about 10 J/cm<sup>2</sup>.
21. The method of Claim 16, wherein the pulse duration of the output beam is between 0.1 and 100 milliseconds
- 15 22. The method of Claim 21, wherein the pulse duration of the output beam is between 1 and 5 milliseconds.
23. A treatment system, comprising:  
a laser source that generates an output beam; and  
an optical system that modifies the output beam to provide a  
20 treatment beam having a non-uniform energy profile, the treatment beam being comprised of a plurality of high-intensity zones surrounded by low-intensity zones within the treatment beam, such that the high-intensity zones heat select portions of the target tissue to a first temperature to shrink

-19-

collagen, while the lower-intensity zones provide sufficient energy to the surrounding tissue to stimulate collagen production.

24. The system of Claim 23, wherein the high-intensity zones heat the tissue to temperatures of 70° C or higher.
- 5 25. The system of Claim 23, wherein the laser source comprises an Nd:YAG laser.
26. The system of Claim 23, wherein the wavelength of the output beam is between about 1.3 microns and 1.6 microns.
27. The system of Claim 26, wherein the wavelength of the output beam is  
10 between about 1.40 and 1.44 microns.
28. The system of Claim 23, wherein the treatment beam at the target tissue area has a diameter between about 7 and 10 mm.
29. The system of Claim 28, wherein the average fluence of the treatment beam at the target tissue area is less than about 10 J/cm<sup>2</sup>.
- 15 30. The system of Claim 23, wherein the output beam has a pulse duration of between 0.1 and 100 milliseconds.
31. The system of Claim 30, wherein the output beam has a pulse duration of between 1 and 5 milliseconds.
32. The system of Claim 23, wherein the optical system comprises a fiber  
20 bundle.

-20-

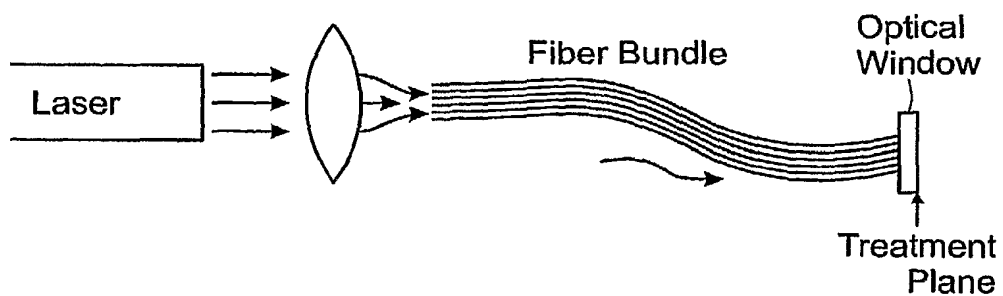
33. The system of Claim 32, wherein the fiber bundle comprises 1000 to 2000 fibers.
34. The system of Claim 32, wherein the optical system comprises a focusing lens for coupling the output beam into a proximal end of the fiber bundle, and an optical window between the distal end of the fiber bundle and the target tissue, the optical window permitting the beam emitted from each fiber in the bundle to diverge before it reaches the target skin so that each beam partially overlaps with the beam(s) from adjacent fibers in the bundle.
35. The system of Claim 34, wherein the optical window is between 1 and 5 mm thick.
36. The system of Claim 32, wherein the average fluence of the treatment beam is less than about 10 J/cm<sup>2</sup>.
37. The system of Claim 32, wherein the optical system comprises a transport fiber that carries the output pulse from the laser source to a handpiece containing the fiber bundle.
38. The system of Claim 23, wherein the optical system comprises a diffractive lens array arranged in an optical path between a laser source and the treatment area, such that each lens in the array provides a high-intensity zone surrounded by a low intensity zone of radiation.
39. The system of Claim 38, wherein the diffractive lens array comprises about 2000 or less lenses in the array.
40. The system of Claim 38, wherein each lens is between about 150 and 450 microns in diameter.

-21-

41. The system of Claim 38, wherein the diffractive lens array is between 7 and 10 millimeters in diameter.
42. The system of Claim 41, wherein the average fluence of the laser output beam is less than about 10 J/cm<sup>2</sup>.
- 5 43. The system of Claim 38, wherein the output beam has a pulse duration of between 0.1 and 100 milliseconds.
44. The system of Claim 38, wherein the pulse duration of the output beam is between 1 and 5 milliseconds.
45. The system of Claim 23, further comprising:
- 10       a tip housing that contains the optical system, a distal end of the tip housing adapted to contact against the target tissue area of the patient; and
- a conduit that carries cooled air to the tip housing, the conduit comprising an outlet that is angled to direct cooled air onto the distal end of the tip housing.
- 15 46. A laser system, comprising:
- a laser source that generates an output beam;
- a fiber bundle comprising a plurality of individual fibers, the fiber bundle having a proximal end and a distal end;
- a focusing lens for coupling the output beam into a proximal end of
- 20 the fiber bundle; and
- an optical window at the distal end of the fiber bundle, the optical window permitting the beams emitted from each fiber in the bundle to diverge as the beam passes through the optical window so that each beam partially overlaps with the beam(s) from adjacent fibers in the bundle.

47. A laser system, comprising:  
a laser source that generates an output beam having an average fluence of less than about 10 J/cm<sup>2</sup>; and  
a diffractive lens array arranged in an optical path between a laser source and a treatment area, such that when the output beam passes through the lens array, a non-uniform treatment beam is produced comprising a plurality of high-intensity zones of radiation surrounded by a contiguous area of lower-intensity radiation.
48. The system of Claim 23, further comprising a pulse light source integrated with the laser source.
49. The system of Claim 48, wherein the pulse light source comprises a flashlamp.
50. The system of Claim 49, wherein the flashlamp comprises a Xenon flashlamp.
51. A treatment system, comprising:  
a laser source that generates an output beam having an average fluence of less than about 10 J/cm<sup>2</sup>;  
a diffractive lens array arranged in an optical path between a laser source and a treatment area, such that when the output beam passes through the lens array, a non-uniform treatment beam is produced comprising a plurality of high-intensity zones of radiation surrounded by a contiguous area of lower-intensity radiation; and  
a pulse light source integrated with the laser source.





Long Fiber Bundle with Optical Window in Contact with the Skin

FIG. 1A

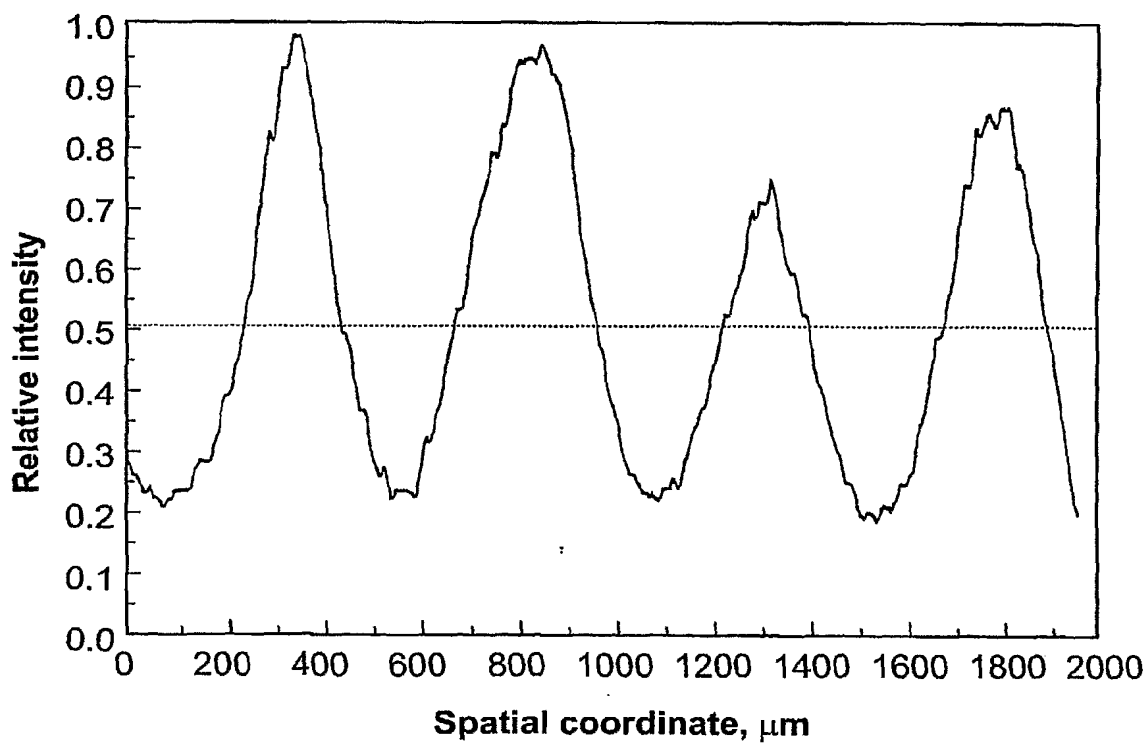


FIG. 1B

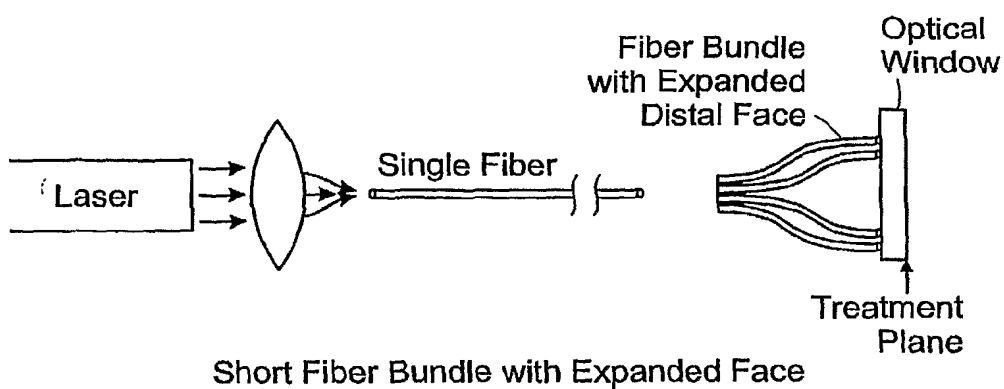
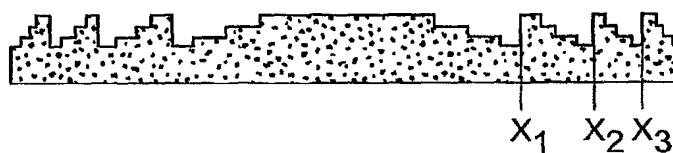
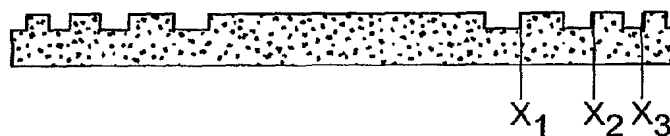


FIG. 2



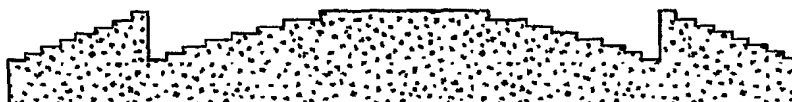
Diffractive Lens with Four Levels

FIG. 3



Diffractive Lens with Two Levels

FIG. 4



Diffractive Lens with Eight Levels

FIG. 5

Diffraction Lens Arrays Arranged in Hexagonal Shapes

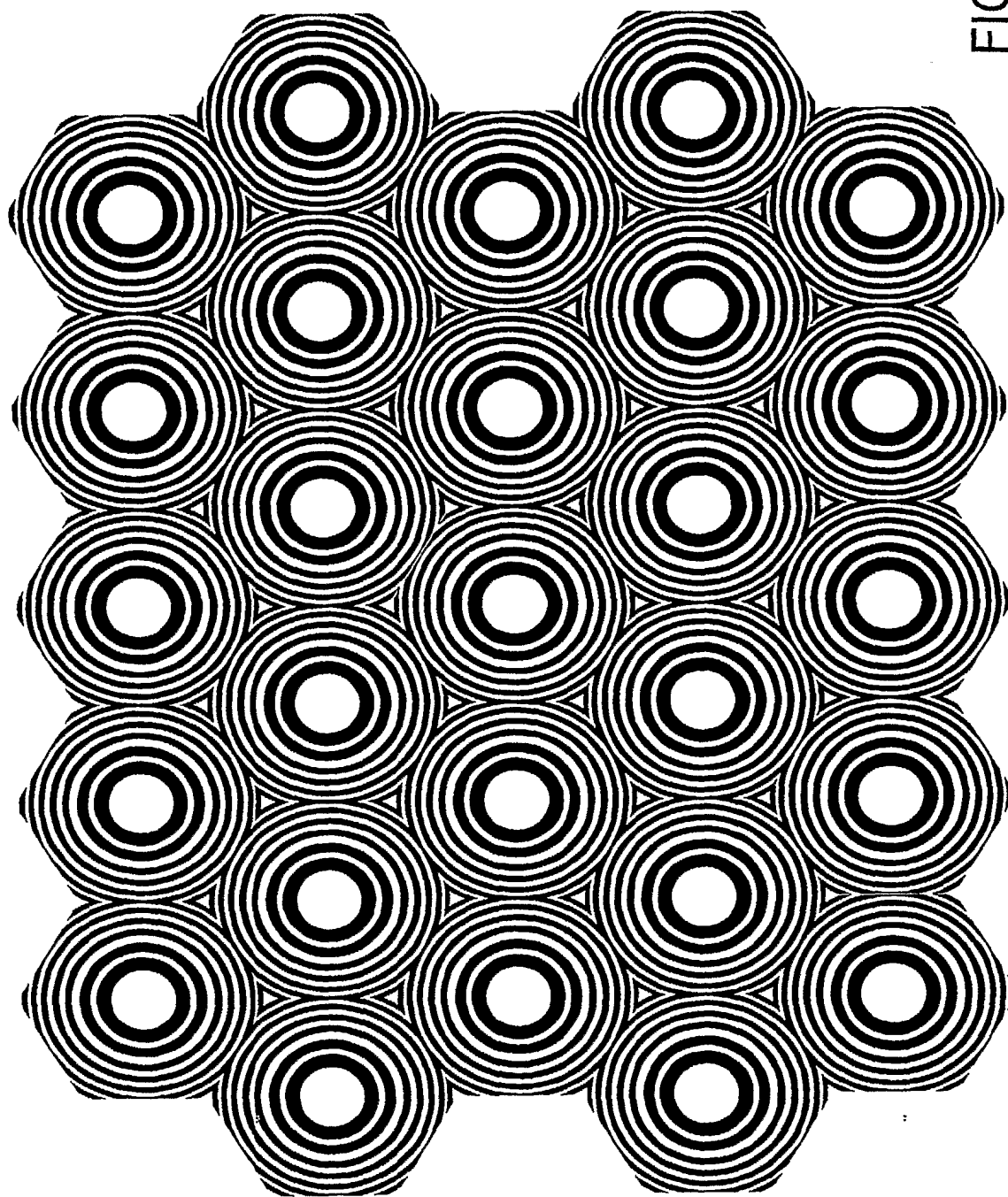


FIG. 6

Diffractive Lens Arrays Arranged in Elongated Hexagonal Shapes

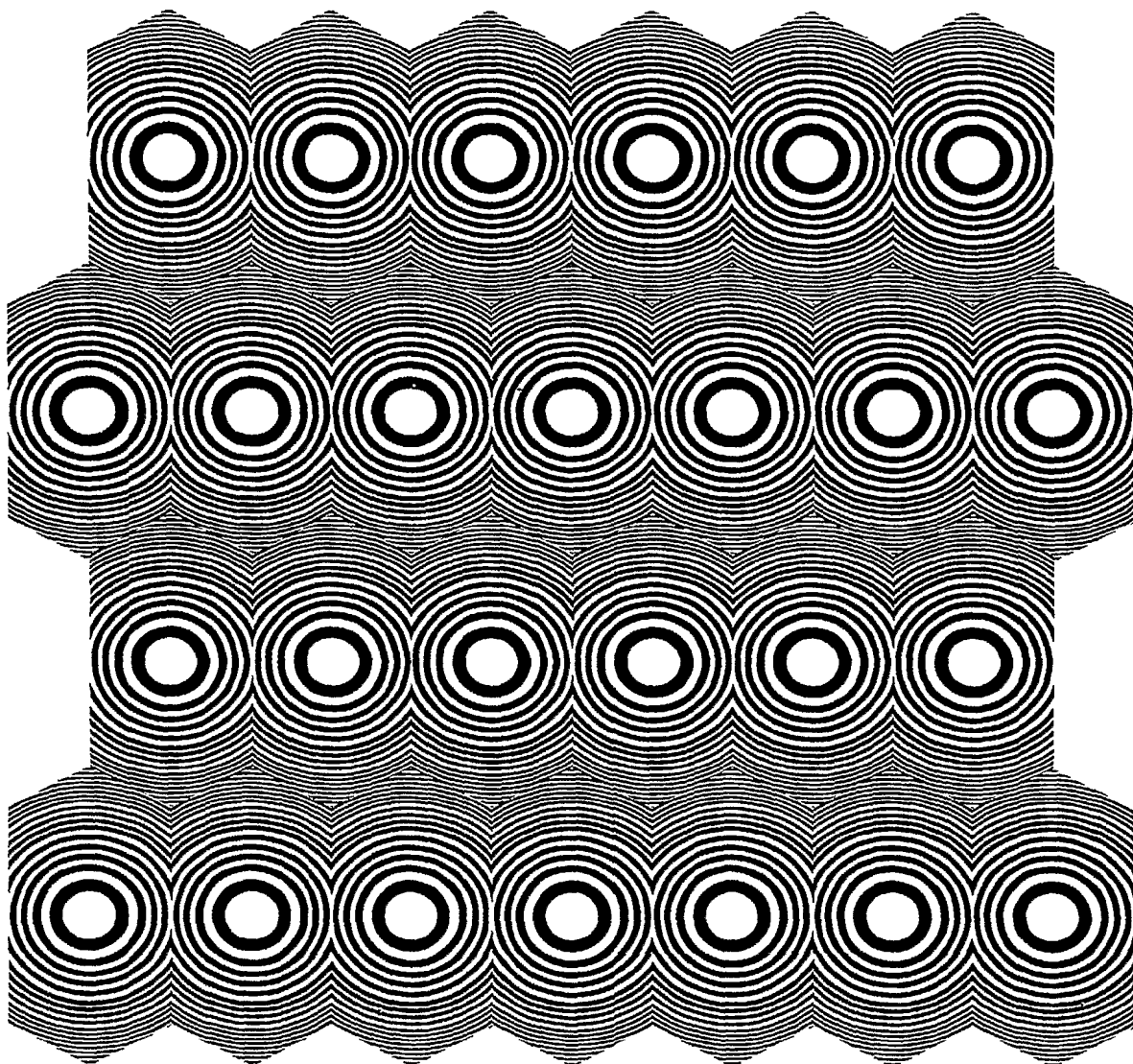


FIG. 7

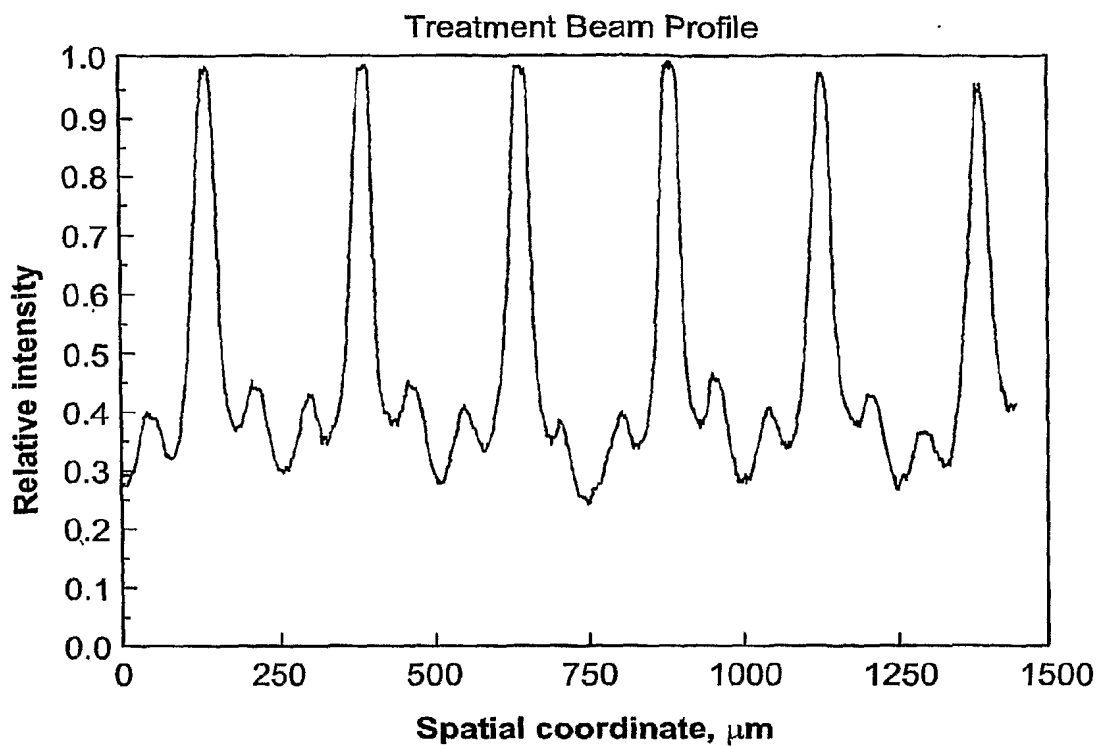


FIG. 8

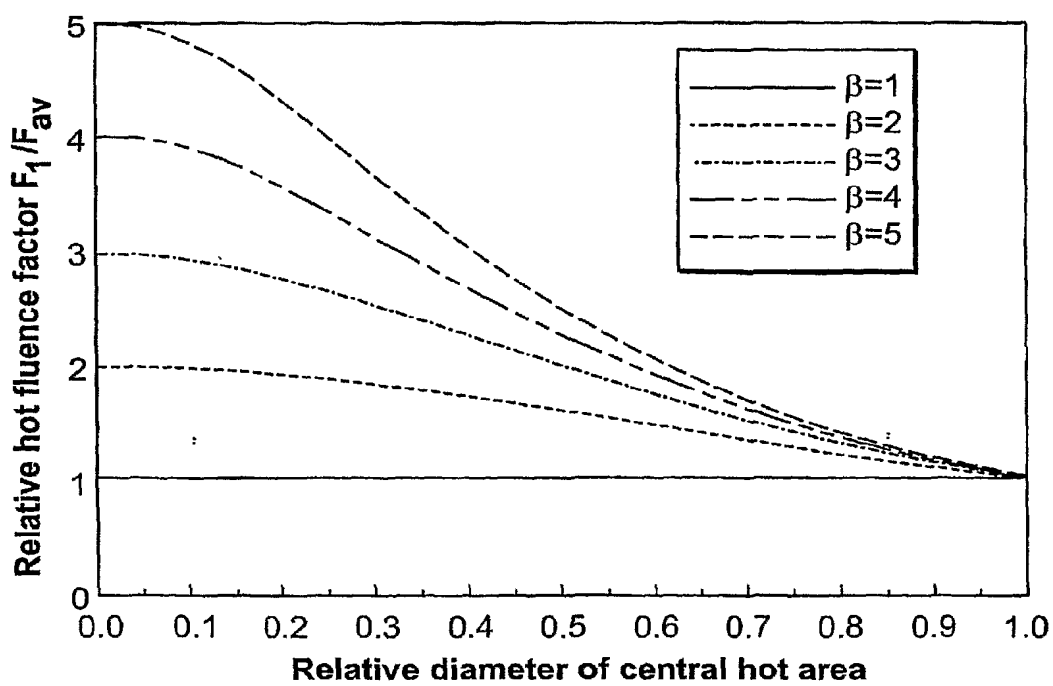
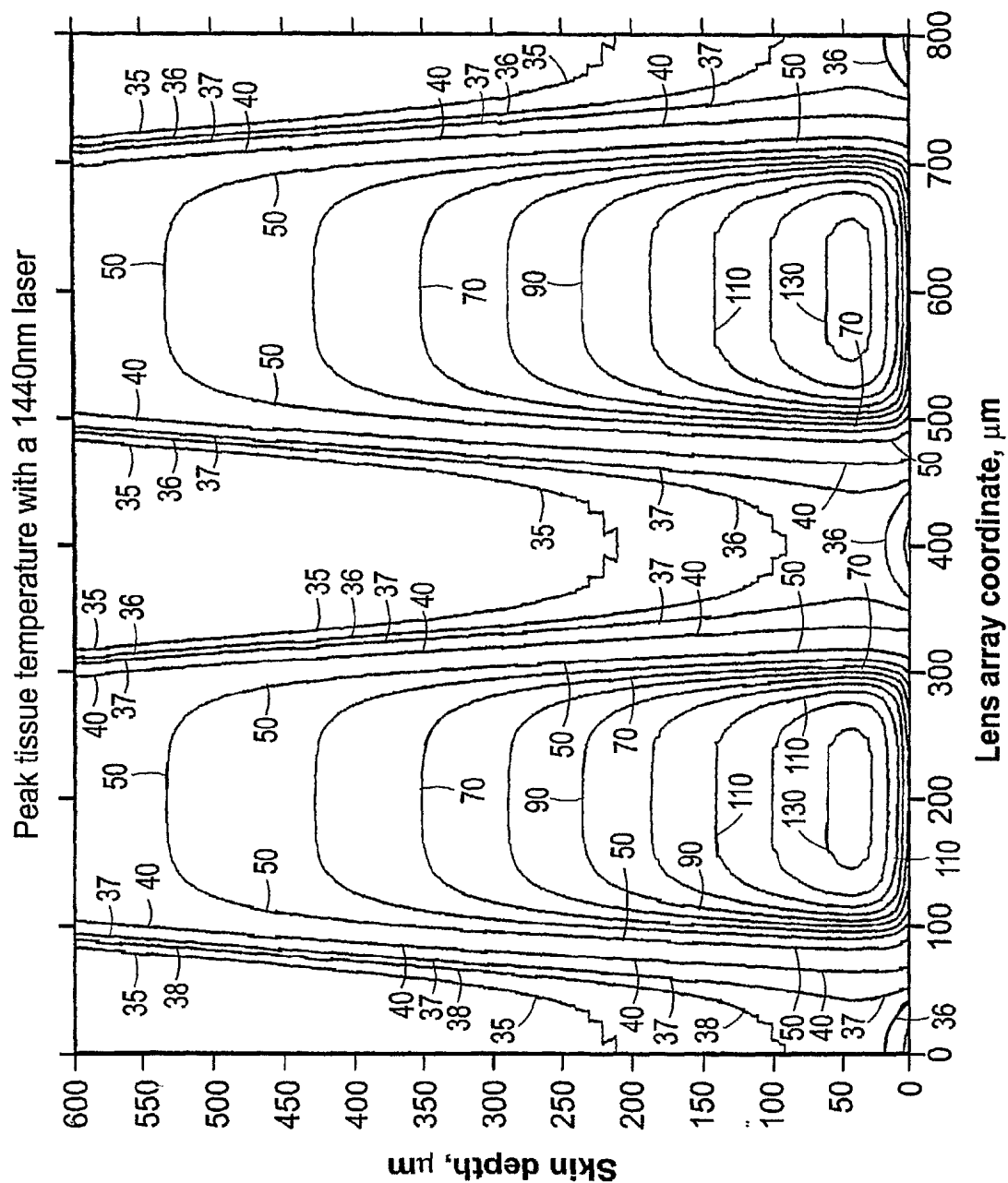


FIG. 9



**Boundary in contact with a glass plate at 32°C, no precooling**  
200 $\mu$ m spot diameter, 22.3J/cm<sup>2</sup> in the dot, 7mJ/dot, 0.83J/cm<sup>2</sup> background, 7J/cm<sup>2</sup> HP fluence, 3ms pulse duration, 90% lens performance, 400 $\mu$ m lens spacing

**FIG. 10**

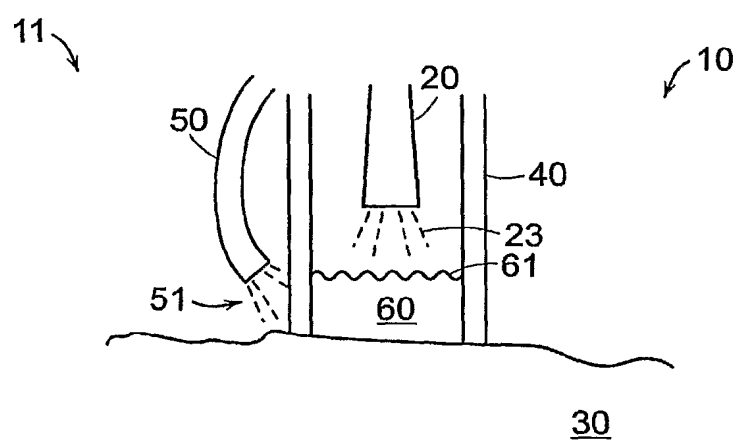


FIG. 11

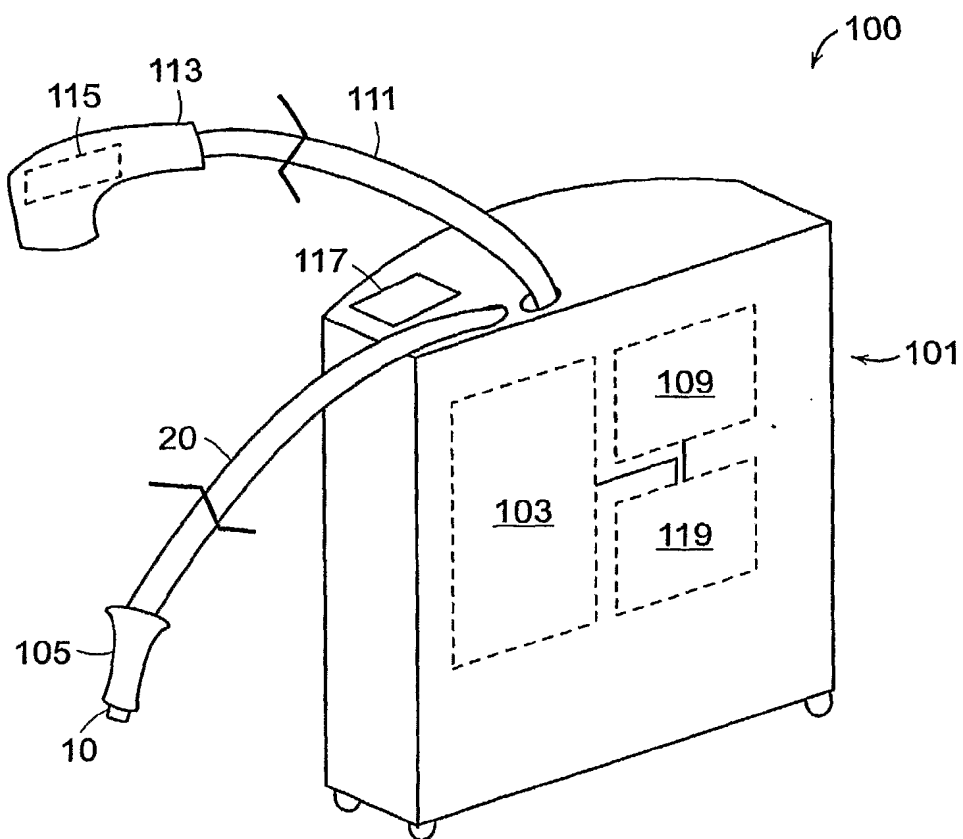


FIG. 12



# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/015180

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. A61N5/067 A61N5/06 A61B18/20		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) A61N A61B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/007003 A (RELIANT TECHNOLOGIES, INC; DEBENDICTIS, LEONARD, C; HERRON, G., SCOTT;) 27 January 2005 (2005-01-27) abstract; claims 12,28,29,32,36,52 paragraph [0094]	23-31, 38-45, 47-51
X	US 6 096 028 A (BAHMANYAR ET AL) 1 August 2000 (2000-08-01)  column 7, line 1 - line 40	23-31, 38-45, 47-51
X	US 2005/080404 A1 (JONES JEFFREY W ET AL) 14 April 2005 (2005-04-14)  paragraphs [0006], [0003], [0032]	23-31, 38-45, 47-51
A	US 2002/151878 A1 (SHIMMICK JOHN KARL ET AL) 17 October 2002 (2002-10-17)  ----- -/--	
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents : *A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *Z* document member of the same patent family		
Date of the actual completion of the international search  1 August 2006		Date of mailing of the international search report  11/08/2006
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Rodríguez Cossío, J

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/015180

Q(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 976 123 A (BAUMGARDNER ET AL) 2 November 1999 (1999-11-02) column 6, line 5 -----	32-37, 46
A	US 2003/040739 A1 (KOOP DALE E) 27 February 2003 (2003-02-27) -----	
A	US 2004/143247 A1 (ANDERSON R. ROX ET AL) 22 July 2004 (2004-07-22) -----	
A	WO 99/39410 A (VISX, INCORPORATED; CAUDLE, GEORGE; LEMBERG, VLADIMIR) 5 August 1999 (1999-08-05) -----	
P, X	WO 2005/099369 A (PALOMAR MEDICAL TECHNOLOGIES, INC; ALTSHULER, GREGORY, B; YAROSLAVSKY,) 27 October 2005 (2005-10-27) the whole document -----	23-51
X	WO 2004/037068 A (RELIANT TECHNOLOGIES, INC) 6 May 2004 (2004-05-06) page 14 - page 16 -----	23, 32-37, 46
A	US 2004/036975 A1 (SLATKINE MICHAEL) 26 February 2004 (2004-02-26) -----	32-37, 46
A	US 2004/210275 A1 (TOWN GODFREY ARTHUR [GB] ET AL) 21 October 2004 (2004-10-21) -----	32-37, 46
A	US 2002/151879 A1 (LOEB MARVIN P) 17 October 2002 (2002-10-17) -----	32-37, 46
A	WO 97/37723 A (NEW STAR LASERS, INC) 16 October 1997 (1997-10-16) -----	32-37, 46
A	US 6 159 203 A (SINOFSKY ET AL) 12 December 2000 (2000-12-12) figures 8,11 -----	32-37, 46
A	US 5 261 904 A (BAKER ET AL) 16 November 1993 (1993-11-16) figure 4 -----	32-37, 46

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2006/015180

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-22  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 23-31,38-45,47-51

treatment system comprising laser source and optical system  
that modifies the output beam to provide an energy profile  
with zones of higher and lower intensity by means of a  
diffractive lens array  
---

2. claims: 23-37,46

treatment system comprising laser source and optical system  
that modifies the output beam to provide an energy profile  
with zones of higher and lower intensity by means of a fiber  
bundle  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/015180

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005007003	A	27-01-2005	EP 1653876 A1	10-05-2006
US 6096028	A	01-08-2000	AU 7729596 A	29-05-1997
			EP 0929255 A1	21-07-1999
			JP 2000500043 T	11-01-2000
			WO 9717011 A1	15-05-1997
			US 6066128 A	23-05-2000
			US 5921981 A	13-07-1999
US 2005080404	A1	14-04-2005	NONE	
US 2002151878	A1	17-10-2002	AU 3612300 A	17-11-2000
			CA 2368228 A1	09-11-2000
			EP 1180981 A1	27-02-2002
			JP 2002542877 T	17-12-2002
			MX PA01010867 A	06-05-2002
			WO 0066022 A1	09-11-2000
US 5976123	A	02-11-1999	US 5820626 A	13-10-1998
US 2003040739	A1	27-02-2003	NONE	
US 2004143247	A1	22-07-2004	DE 69830732 D1	04-08-2005
			DE 69830732 T2	04-05-2006
			EP 1011811 A1	28-06-2000
			WO 9833558 A1	06-08-1998
			US 2005256515 A1	17-11-2005
			US 6120497 A	19-09-2000
			US 6659999 B1	09-12-2003
			US 5810801 A	22-09-1998
WO 9939410	A	05-08-1999	AT 291787 T	15-04-2005
			AU 2560499 A	16-08-1999
			CA 2319122 A1	05-08-1999
			DE 69924358 D1	28-04-2005
			DE 69924358 T2	19-01-2006
			EP 1051781 A1	15-11-2000
			JP 2002502062 T	22-01-2002
WO 2005099369	A	27-10-2005	NONE	
WO 2004037068	A	06-05-2004	AU 2003284336 A1	13-05-2004
			AU 2003286609 A1	13-05-2004
			BR 0314913 A	30-08-2005
			CA 2502619 A1	06-05-2004
			EP 1571972 A2	14-09-2005
			EP 1585432 A2	19-10-2005
			JP 2006503681 T	02-02-2006
			WO 2004037069 A2	06-05-2004
US 2004036975	A1	26-02-2004	AU 2002321806 A1	23-06-2003
			EP 1455671 A1	15-09-2004
			WO 03049633 A1	19-06-2003
			JP 2005511196 T	28-04-2005
			US 2006013533 A1	19-01-2006
			US 2005234527 A1	20-10-2005
US 2004210275	A1	21-10-2004	WO 02089689 A1	14-11-2002

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/015180

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004210275 A1		EP 1387643 A1	11-02-2004
US 2002151879 A1	17-10-2002	NONE	
WO 9737723 A	16-10-1997	AU 2318197 A	29-10-1997
US 6159203 A	12-12-2000	US 4950266 A	21-08-1990
US 5261904 A	16-11-1993	NONE	